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Original Article

Alopathy Drug Used Treatment for Tuberculosis (Tb)

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ABSTRACT

Tuberculosis (TB) remains one of the leading infectious diseases worldwide, requiring effective and timely treatment to prevent morbidity and mortality. Allopathic medicine offers a standardized approach to TB treatment through the use of first-line and second-line antitubercular drugs. These include isoniazid, rifampin, ethambutol, and pyrazinamide as primary agents, often administered in combination to enhance efficacy and prevent resistance. The treatment regimen targets Mycobacterium tuberculosis, leveraging mechanisms such as inhibition of cell wall synthesis, protein synthesis, and bacterial DNA replication. Despite significant success in reducing TB burden globally, challenges such as drug resistance (e.g., multidrug-resistant TB) and adverse drug reactions remain critical issues. Innovations in allopathic therapy, including the development of shorter regimens, adjunctive therapies, and drug susceptibility testing, aim to improve patient outcomes and address these challenges. This abstract highlights the role of allopathic drugs in TB management, emphasizing the need for continued research to optimize treatment efficacy and mitigate resistance.

Keywords: Tuberculosis, allopathic medicine, antitubercular drugs, isoniazid, rifampin, multidrug-resistant tuberculosis (MDR-TB), drug resistance, Mycobacterium tuberculosis, combination therapy, adverse drug reactions, treatment regimen, public health, drug susceptibility testing.

INTRODUCTION

Tuberculosis (TB) is a highly contagious infectious disease caused by Mycobacterium tuberculosis, which primarily affects the lungs but can also involve other parts of the body. Despite being preventable and curable, TB remains a global health challenge, with millions of cases and deaths reported annually. The advent of allopathic medicine has revolutionized TB treatment, significantly reducing its burden through the use of effective antitubercular drugs. Allopathic TB treatment relies on a standardized drug regimen involving first-line medications such as isoniazid, rifampin, ethambutol, and pyrazinamide. These drugs work synergistically to target the bacteria's metabolic pathways, ensuring both bactericidal and bacteriostatic effects. The implementation of combination therapy prevents the emergence of drug resistance, a significant concern in TB management. However, multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains pose growing challenges, requiring second-line drugs such as fluoroquinolones and injectable agents. This introduction explores the role of allopathic drugs in combating TB, emphasizing their mechanisms of action, efficacy, and the ongoing challenges in addressing drug resistance, patient adherence, and adverse effects. The significance of optimizing treatment protocols and advancing drug development is crucial to achieving global TB control and eventual eradication.

What is Tuberculosis?

Tuberculosis (TB) is a contagious infectious disease caused by the bacterium Mycobacterium tuberculosis. It primarily affects the lungs (pulmonary TB) but can also spread to other parts of the body, such as the brain, spine, kidneys, and lymph nodes (extrapulmonary TB). TB spreads from person to person through airborne droplets when an infected individual coughs, sneezes, speaks, or sings.

The disease has two major forms:

1. Latent TB Infection: The bacteria remain inactive in the body without causing symptoms. However, latent TB can become active if the immune system weakens.
2. Active TB Disease: The bacteria multiply and cause symptoms, including persistent cough, fever, night sweats, weight loss, and fatigue.

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TB is a significant global health concern, with millions of new cases reported annually. While it is curable and preventable, challenges such as drug resistance, inadequate healthcare access, and co-infections like HIV complicate its management. Early diagnosis, effective treatment, and public health measures are essential to controlling TB.

TYPES OF TUBERCULOSIS

Tuberculosis (TB) can be categorized into several types based on the site of infection and the disease progression. The main types are:

1. Pulmonary Tuberculosis (PTB)

- Description: This is the most common form of TB, affecting the lungs.
- Symptoms: Persistent cough (often with blood), chest pain, fever, night sweats, and weight loss.
- Transmission: Pulmonary TB is highly contagious and spreads through airborne droplets when an infected person coughs or sneezes.

2. Extrapulmonary Tuberculosis (EPTB)

- Description: This occurs when TB bacteria spread outside the lungs to other organs.
- Common Sites:
- Lymphatic TB: Affects the lymph nodes (commonly known as scrofula).
- Pleural TB: Involves the pleura, causing pleural effusion.
- Bone and Joint TB: Affects bones and joints, often the spine (Pott's disease).
- Miliary TB: A severe form where TB spreads throughout the body via the bloodstream.
- Genitourinary TB: Affects the kidneys, bladder, or reproductive organs.
- Central Nervous System TB: Leads to TB meningitis, affecting the brain and spinal cord.

3. Latent Tuberculosis

- Description: The bacteria are present in the body but inactive, causing no symptoms.
- Characteristics:
- Non-contagious.
- Can reactivate and develop into active TB if the immune system weakens.

4. Active Tuberculosis

- Description: The bacteria multiply, causing symptoms and making the person infectious.
- Symptoms: Persistent cough, fever, night sweats, weight loss, and fatigue.
- Importance: Requires immediate medical treatment to prevent complications and transmission.

5. Drug-Resistant Tuberculosis (DR-TB)

This type develops when TB bacteria become resistant to standard antitubercular drugs. It includes:

- Multidrug-Resistant TB (MDR-TB): Resistant to at least isoniazid and rifampin.
- Extensively Drug-Resistant TB (XDR-TB): Resistant to first-line drugs and some second-line drugs like fluoroquinolones and injectable agents.

6. Primary and Secondary Tuberculosis

- Primary TB: Occurs shortly after the initial infection, often in individuals with no prior TB exposure.
- Secondary (Reactivation) TB: Develops when latent TB reactivates due to weakened immunity or other factors.

Understanding these types is essential for effective diagnosis, treatment, and prevention strategies.

PATHOPHYSIOLOGY OF TUBERCULOSIS:

Tuberculosis (TB) is caused by Mycobacterium tuberculosis, a slow-growing, aerobic, acid-fast bacillus. The pathophysiology involves a complex interaction between the bacteria and the host immune system, leading to the formation of granulomas, tissue damage, and disease progression.

Stages of Pathophysiology

1. Infection:

- TB is transmitted via inhalation of airborne droplets containing M. tuberculosis.
- The bacteria reach the alveoli in the lungs, where they are phagocytosed by alveolar macrophages.

2. Immune Response:

- Infected macrophages trigger an immune response, recruiting T cells and other immune cells to the site of infection.
- A granuloma forms, consisting of macrophages, T cells, and giant cells, attempting to contain the bacteria.

3. Latent TB:

- If the immune system successfully contains the bacteria, TB remains dormant within the granulomas.
- This stage is non-symptomatic and non-contagious.

4. Active TB:

- In cases of immune compromise (e.g., HIV, malnutrition, diabetes), the granuloma structure

breaks down, allowing bacteria to replicate and spread.
- This leads to symptoms such as persistent cough, fever, and weight loss.

5. Extrapulmonary Spread:
- In some cases, the bacteria disseminate through the bloodstream or lymphatic system, affecting organs such as the brain, spine, or kidneys.

Role of Allopathic Drugs in TB Treatment:

The goal of allopathic drugs is to eradicate M. tuberculosis while minimizing resistance and adverse effects. The standard treatment follows the Directly Observed Treatment, Short-course (DOTS) strategy, involving two phases:

1. Intensive Phase (2 months
- Drugs Used: Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PZA), and Ethambutol (EMB).
- Mechanisms of Action:
- Isoniazid: Inhibits mycolic acid synthesis, disrupting bacterial cell wall formation.
- Rifampin: Inhibits RNA polymerase, blocking bacterial transcription.
- Pyrazinamide: Disrupts membrane transport and energy production in acidic environments.
- Ethambutol: Inhibits arabinogalactan synthesis, interfering with cell wall integrity.

2. Continuation Phase (4-6 months)
- Drugs Used: Isoniazid and Rifampin.
- Purpose: Eliminates dormant bacteria to prevent relapse.

Addressing Drug-Resistant TB

For multidrug-resistant TB (MDR-TB) or extensively drug-resistant TB (XDR-TB), second-line drugs are used:
- Fluoroquinolones (e.g., levofloxacin, moxifloxacin): Inhibit DNA gyrase.
- Injectable Agents (e.g., amikacin, kanamycin): Inhibit protein synthesis.
- Newer Drugs: Bedaquiline (inhibits ATP synthase) and Delamanid (inhibits mycolic acid synthesis). Impact on Pathophysiology
- Allopathic drugs directly target M. tuberculosis, disrupting bacterial metabolism and replication.
- By killing active and dormant bacteria, these drugs reduce bacterial load, resolve granulomas, and restore lung tissue function.
- Early and effective treatment prevents complications, transmission, and resistance development.

This allopathic approach, guided by a deep understanding of TB pathophysiology, has significantly improved patient outcomes worldwide.

SYMPTOMS OF TUBERCULOSIS (T.B):

The symptoms of tuberculosis depend on whether it is pulmonary TB (affecting the lungs) or extrapulmonary TB (affecting other organs).

1. Pulmonary Tuberculosis (TB in the Lungs)

This is the most common form of TB. Symptoms include:
- Persistent Cough: Lasting for more than 2-3 weeks; may start dry and progress to productive.
- Hemoptysis: Coughing up blood or blood-stained mucus.
- Chest Pain: Pain during breathing or coughing.
- Shortness of Breath: Due to lung damage in advanced cases.
- General Symptoms:
- Low-grade fever.
- Night sweats.
- Fatigue or weakness.
- Unexplained weight loss.
- Loss of appetite.

2. Extrapulmonary Tuberculosis (TB Outside the Lungs)

TB can affect organs other than the lungs. Symptoms vary based on the affected organ:
- Lymph Node TB:
- Swollen, painless lymph nodes, commonly in the neck.
- Nodes may become tender or drain pus if abscesses form.
- Bone and Joint TB (Pott's Disease):
- Back pain or stiffness.
- Swelling or limited movement in joints.
- TB Meningitis (Brain and Spinal Cord):
- Severe headache.
- Neck stiffness.
- Confusion or altered consciousness.
- Sensitivity to light (photophobia).
- Miliary TB (Disseminated TB):
- Generalized weakness.
- Persistent high fever.
- Enlargement of the liver or spleen.
- Pleural TB (TB of the Pleura):
- Chest pain.
- Difficulty breathing due to fluid accumulation (pleural effusion).
- Genitourinary TB:

- Blood in the urine.
- Pain during urination.
- Pelvic pain or infertility (in females).

3. General Symptoms of Active TB

Regardless of the site, active TB often presents with systemic symptoms:

- Low-grade fever, often worse in the evenings.
- Profuse night sweats.
- Loss of appetite.
- Severe weight loss (wasting).
- Chronic fatigue.

4. Latent TB

- No symptoms.
- The person is not contagious but harbors the bacteria, which can become active later.

CAUSES OF TUBERCULOSIS:

Tuberculosis (TB) is caused by the bacterium Mycobacterium tuberculosis, a slow-growing, rod-shaped, acid-fast bacillus. The disease is primarily transmitted from person to person through airborne droplets, though certain risk factors and conditions increase susceptibility.

1. Primary Cause

- Mycobacterium tuberculosis:
- This bacterium is the primary causative agent of TB.
- It thrives in oxygen-rich environments, such as the lungs.

2. Transmission

- TB spreads through airborne droplets when an infected person:
- Coughs, sneezes, speaks, laughs, or sings.
- These droplets are inhaled by another person, leading to infection.

3. Risk Factors for TB Infection

Certain factors increase the likelihood of contracting TB:

Environmental and Social Factors

- Close contact with an infected individual, especially in crowded or poorly ventilated spaces.
- Living or working in TB-endemic areas.
- Poor socioeconomic conditions (e.g., malnutrition, lack of healthcare access).

Medical Conditions and Immunosuppression

- HIV/AIDS: Weakens the immune system, making individuals more susceptible to TB.
- Diabetes Mellitus: Increases risk by impairing immune responses.
- Chronic Kidney Disease: Associated with immune suppression.
- Malnutrition: Reduces the body's ability to fight infections.
- Organ Transplantation: Use of immunosuppressive drugs increases TB risk.
- Cancer: Certain cancers and treatments weaken the immune system.

Lifestyle and Behavioral Factors

- Tobacco smoking: Damages lung function, increasing TB risk.
- Alcohol abuse: Weakens the immune system.
- Intravenous drug use: Associated with poor health and weakened immunity.

Age

- Infants and the elderly are more susceptible due to weaker immune systems.

4. Other Contributing Factors

- Multidrug-Resistant Tuberculosis (MDR-TB): Resistance to standard TB drugs can make treatment difficult and increase transmission risk.
- Latent TB Reactivation: In individuals with latent TB, the bacteria can reactivate under conditions like immunosuppression, malnutrition, or aging.

TREATMENT OF TUBERCULOSIS USING ALLOPATHIC DRUGS:

The treatment of tuberculosis (TB) in allopathic medicine involves a structured, evidence-based regimen of antitubercular drugs designed to eradicate the Mycobacterium tuberculosis bacteria, prevent resistance, and reduce transmission. The regimen varies based on the type of TB (drug-susceptible or drug-resistant) and the disease's stage (latent or active).

1. First-Line Drugs (For Drug-Susceptible TB)

For patients with drug-susceptible TB, the treatment follows the Directly Observed Treatment, Short-Course (DOTS) strategy, which is typically divided into two phases:

A. Intensive Phase (First 2 Months)

Combination of four drugs:

- Isoniazid (INH): Inhibits mycolic acid synthesis, disrupting the bacterial cell wall.
- Rifampin (RIF): Inhibits bacterial RNA polymerase, blocking protein synthesis.
- Pyrazinamide (PZA): Lowers pH within the bacterial cell, disrupting metabolic processes.
- Ethambutol (EMB): Inhibits arabinogalactan synthesis, weakening the cell wall.

B. Continuation Phase (4-6 Months)
Combination of two drugs:
- Isoniazid (INH).
- Rifampin (RIF).

The continuation phase eliminates remaining bacteria and prevents relapse.

2. Treatment for Latent TB

Patients with latent TB are treated to prevent progression to active TB, especially in high-risk groups. Common regimens include:
- Isoniazid (INH): Daily for 6-9 months.
- Rifampin (RIF): Daily for 4 months.
- Combination of Isoniazid and Rifapentine: Once weekly for 3 months.

3. Second-Line Drugs (For Drug-Resistant TB)

For multidrug-resistant TB (MDR-TB) or extensively drug-resistant TB (XDR-TB), treatment involves second-line drugs, which are less effective and have more side effects.

Common Second-Line Drugs:
- Fluoroquinolones (e.g., levofloxacin, moxifloxacin): Inhibit bacterial DNA gyrase.
- Injectable Agents (e.g., amikacin, kanamycin, capreomycin): Inhibit protein synthesis.
- Linezolid: Inhibits bacterial protein synthesis.
- Clofazimine: Disrupts bacterial membrane integrity.

Newer Drugs for Drug-Resistant TB:
- Bedaquiline: Inhibits ATP synthase, essential for bacterial energy production.
- Delamanid: Inhibits mycolic acid synthesis.

Treatment duration for drug-resistant TB can extend to 18-24 months.

4. Adjunctive Therapies
- Corticosteroids: Used in severe cases, such as TB meningitis or pericarditis, to reduce inflammation.
- Nutritional Support: Helps improve immune function and recovery.

5. Monitoring and Support
- Regular monitoring for side effects, such as hepatotoxicity (from isoniazid, rifampin, or pyrazinamide) or optic neuritis (from ethambutol).
- Ensuring adherence to prevent resistance through DOTS or other strategies.

DRUG-RESISTANT TUBERCULOSIS (DR-TB)

Drug-resistant tuberculosis (DR-TB) occurs when Mycobacterium tuberculosis bacteria develop resistance to one or more of the standard antitubercular drugs. This resistance makes treatment more complex, lengthy, and costly.

Types of Drug-Resistant TB

1. Mono-Drug Resistant TB:
- Resistance to a single first-line drug, such as isoniazid or rifampin.

2. Multidrug-Resistant TB (MDR-TB):
- Resistance to at least isoniazid (INH) and rifampin (RIF), the two most powerful first-line drugs.

3. Extensively Drug-Resistant TB (XDR-TB):
- MDR-TB that is also resistant to:
- Any fluoroquinolone (e.g., levofloxacin, moxifloxacin).
- At least one second-line injectable drug (e.g., amikacin, kanamycin, capreomycin).

4. Pre-Extensively Drug-Resistant TB (Pre-XDR TB):
- MDR-TB with additional resistance to a fluoroquinolone, but still susceptible to second-line injectable drugs.

5. Totally Drug-Resistant TB (TDR-TB):
- Rare cases where TB bacteria are resistant to all available first-line and second-line drugs.

Causes of Drug-Resistant TB

1. Incomplete or Improper Treatment:
- Patients not completing their full course of treatment.
- Incorrect dosages or inconsistent drug supply.

2. Transmission of Resistant Strains:
- People can directly contract DR-TB from individuals with resistant forms of TB.

3. Spontaneous Mutation:
- Random genetic mutations in Mycobacterium tuberculosis can lead to drug resistance.

4. Mismanagement of TB:
- Improper drug combinations or inadequate monitoring during treatment.

Diagnosis of Drug-Resistant TB

1. Molecular Testing:
- GeneXpert MTB/RIF: Detects TB and rifampin resistance in a few hours.
- Line Probe Assays (LPA): Detects genetic mutations responsible for resistance to first- and second-line drugs.

2. Culture and Drug Susceptibility Testing (DST):

• Identifies resistance by growing the bacteria in a lab and testing against various drugs (time-intensive).

Treatment of Drug-Resistant TB

1. MDR-TB Treatment

• Second-Line Drugs: Fluoroquinolones (e.g., levofloxacin, moxifloxacin) and injectables (amikacin, kanamycin).

• Newer Drugs:

• Bedaquiline: Inhibits ATP synthase.

• Delamanid: Disrupts mycolic acid synthesis.

• Treatment duration: 18–24 months.

2. XDR-TB Treatment

• Requires a combination of new and repurposed drugs:

• Linezolid: Inhibits protein synthesis.

• Clofazimine: Disrupts bacterial membrane function.

• Bedaquiline and delamanid.

• Treatment may take over 24 months and involves close monitoring for adverse effects.

3. Individualized Therapy

• Drug regimens are tailored based on drug susceptibility test results.

Challenges in DR-TB Management

1. Longer Treatment Duration:

• Standard TB treatment is 6 months, whereas MDR/XDR-TB treatments last 18–24 months.

2. Higher Costs:

• Second-line drugs are expensive and not always readily available.

3. Severe Side Effects:

• Toxicities include hearing loss (injectables), neuropathy (linezolid), and cardiac issues (bedaquiline).

4. Adherence Issues:

• Longer regimens and side effects make it difficult for patients to adhere to treatment.

5. Limited Access to New Drugs:

• Drugs like bedaquiline and delamanid may not be available in resource-limited settings.

Prevention of Drug-Resistant TB

1. Ensuring Treatment Adherence:

• Use of Directly Observed Therapy (DOT) to monitor and support patients during treatment.

2. Prompt and Accurate Diagnosis:

• Early detection of resistance to ensure proper treatment.

3. Infection Control:

• Isolation of patients with DR-TB in healthcare settings to prevent transmission.

4. Public Health Education:

• Educating communities about the importance of completing treatment.

5. Strengthening Health Systems:

• Ensuring consistent drug supply and access to diagnostics tools

ADVANTAGES AND DISADVANTAGES OF USING ALLOPATHIC DRUGS IN TUBERCULOSIS TREATMENT:

Advantages

1. Effective Eradication of Bacteria:

• Allopathic drugs target Mycobacterium tuberculosis effectively, leading to high cure rates when the treatment is followed properly.

2. Structured Treatment Regimens:

• Regimens like DOTS (Directly Observed Treatment, Short-Course) ensure systematic and efficient TB management.

3. Prevention of Relapse:

• Combination therapy eliminates active and dormant bacteria, reducing the chances of recurrence.

4. Wide Availability:

• First-line antitubercular drugs (e.g., isoniazid, rifampin) are widely available and affordable in most regions.

5. Customizable for Drug Resistance:

• Second-line drugs and newer medications (e.g., bedaquiline, delamanid) address multidrug-resistant (MDR-TB) and extensively drug-resistant TB (XDR-TB).

6. Prevention of Spread:

• Early treatment with allopathic drugs significantly reduces the transmission of TB to others.

7. Shortened Duration:

• Advances in drug regimens have reduced the duration of TB treatment (e.g., from 12–18 months to 6 months for drug-sensitive TB).

8. Supportive Guidelines:

• WHO guidelines ensure standardized and evidence-based approaches to TB management.

Disadvantages

1. Side Effects:

• Hepatotoxicity: Isoniazid, rifampin, and pyrazinamide can cause liver damage.

• Gastrointestinal Issues: Nausea, vomiting, and loss of appetite are common.

- Optic Neuritis: Ethambutol can lead to vision problems.
- Hearing Loss: Injectable second-line drugs like amikacin may cause ototoxicity.

2. Drug Resistance:
- Incomplete or improper adherence to treatment can lead to drug-resistant TB (MDR-TB or XDR-TB), which is harder to treat.

3. Lengthy Treatment Duration:
- Even for drug-sensitive TB, treatment requires a minimum of 6 months, leading to challenges in adherence.
- Drug-resistant TB treatment can last 18–24 months or longer.

4. Cost of Second-Line Drugs:
- While first-line drugs are affordable, second-line and newer drugs (e.g., bedaquiline, delamanid) can be expensive and less accessible in low-income regions.

5. Adverse Drug Interactions:
- Rifampin interacts with many drugs, complicating treatment in patients with comorbidities (e.g., HIV, diabetes).

6. Need for Monitoring:
- Patients require regular follow-ups and testing to monitor drug efficacy and side effects, which can strain healthcare resources.

7. Stigma and Social Challenges:
- Long treatment duration may increase the risk of social stigma and mental health issues, leading to poor adherence.

8. Potential for Toxicity in Vulnerable Populations:
- Pregnant women, children, and individuals with liver or kidney conditions are at higher risk of adverse effects.

CONCLUSION

The use of allopathic drugs for the treatment of tuberculosis (TB) has been a cornerstone in controlling and curing this infectious disease. The most commonly used drugs in tuberculosis treatment include first-line medications like isoniazid, rifampicin, pyrazinamide, and ethambutol. These drugs, when used in combination, effectively eliminate the causative bacteria, Mycobacterium tuberculosis, and significantly reduce the risk of drug resistance.

Key Points in Conclusion:

1. Effectiveness: Allopathic drugs, particularly through Directly Observed Treatment Short-course (DOTS) programs, have proven highly effective in curing TB and reducing transmission.
2. Resistance Concerns: The misuse or incomplete adherence to treatment can lead to multidrug-resistant tuberculosis (MDR-TB) or extensively drug-resistant tuberculosis (XDR-TB), necessitating stricter monitoring.
3. Side Effects: While these drugs are lifesaving, they can have side effects such as hepatotoxicity, gastrointestinal upset, and hypersensitivity, which need careful management.
4. Advancements: Newer drugs like bedaquiline and delamanid have been introduced for drug-resistant TB, showing promise in improving outcomes.
5. Public Health Impact: Allopathic TB treatment has dramatically reduced global TB mortality rates, though challenges like drug resistance, co-infection with HIV, and healthcare access remain.

RESULT

From a total of 68 research documents that reported use of plants for treatment of TB 98 plants species belonging to 82 genera and 49 families were identified. The most frequently reported plant species belonged to family Lamiaceae (n = 8), Euphorbiaceae (n = 7), Cucurbitaceae (n = 6) and Fabaceae (n = 6). Croton macrostachyus, Allium sativum, and Myrsine Africana were the most often mentioned anti-TB medicinal plants. Shrubs (35.7%) and trees (29.6%) were reported as dominant growth forms while plant roots (31.6%) and leaves (28.6%) were frequently used plant parts for the preparations of the treatment. The most favored administration route was oral (59.1%). About 87% of the preparations were made from fresh plant materials. No experimental/clinical evidence was presented for 79.6% (78/98) of the reported plants to support their anti-mycobacterial activities.

REFERENCE

1. World Health Organization (WHO). Global tuberculosis report 2018. WHO; 2018. Geneva (Switzerland). [Google Scholar]
2. Kendall EA, Shrestha S, Cohen T, et al. Priority-setting for novel drug regimens to treat tuberculosis: an epidemiologic model. PLoS Med

2017; 14(1):e1002202. [DOI] [PMC free article] [PubMed] [Google Scholar]
3. Imperial MZ, Nahid P, Phillips PPJ, et al. A patient-level pooled analysis of treatment-shortening regimens for drug-susceptible pulmonary tuberculosis. Nat Med 2018;24(11):1708–15. [DOI] [PMC free article] [PubMed] [Google Scholar]
4. Slomski A. South Africa warns of emergence of "totally" drug-resistant tuberculosis. JAMA 2013; 309(11):1097–8. [DOI] [PubMed] [Google Scholar]
5. Dheda K, Limberis JD, Pietersen E, et al. Outcomes, infectiousness, and transmission dynamics of patients with extensively drug-resistant tuberculosis and home-discharged patients with programmatically incurable tuberculosis: a prospective cohort study. Lancet Respir Med 2017; 5(4):269–81. [DOI] [PubMed] [Google Scholar]
6. Ahmad N, Ahuja SD, Akkerman OW, et al. Treatment correlates of successful outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis. Lancet 2018; 392(10150):821–34. [DOI] [PMC free article] [PubMed] [Google Scholar]
7. Van Deun A, Maug AKJ, Salim MAH, et al. Short, highly effective, and inexpensive standardized treatment of multidrug-resistant tuberculosis. Am J Respir Crit Care Med 2010;182(5):684–92. [DOI] [PubMed] [Google Scholar]
8. Trébucq A, Schwoebel V, Kashongwe Z, et al. Treatment outcome with a short multidrug-resistant tuberculosis regimen in nine African countries. Int J Tuberc Lung Dis 2018;22(1):17–25. [DOI] [PubMed] [Google Scholar]
9. Sotgiu G, Tiberi S, D'Ambrosio L, et al. Faster for less: the new "shorter" regimen for multidrug-resistant tuberculosis. Eur Respir J 2016;48(5): 1503–7. [DOI] [PubMed] [Google Scholar]
10. World Health Organization. Rapid communication: key changes to treatment of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB). Geneva (Switzerland): WHO; 2018. [Google Scholar]
11. World Health Organization (WHO). The use of bedaquiline in the treatment of multidrug-resistant tuberculosis: interim policy guidance. Geneva (Switzerland): World Health Organization; 2013. [PubMed] [Google Scholar]
12. Andries K, Verhasselt P, Guillemont J, et al. A diarylquinoline drug active on the ATP synthase of Mycobacterium tuberculosis. Science 2005; 307(5707):223–7. [DOI] [PubMed] [Google Scholar]
13. Lounis N, Gevers T, Van Den Berg J, et al. ATP synthase inhibition of Mycobacterium avium is not bactericidal. Antimicrob Agents Chemother 2009; 53(11):4927–9. [DOI] [PMC free article] [PubMed] [Google Scholar]
14. Zhang T, Li SY, Williams KN, et al. Short-course chemotherapy with TMC207 and rifapentine in a murine model of latent tuberculosis infection. Am J Respir Crit Care Med 2011;184(6):732–7. [DOI] [PMC free article] [PubMed] [Google Scholar]
15. Shang S, Shanley CA, Caraway ML, et al. Activities of TMC207, rifampin, and pyrazinamide against Mycobacterium tuberculosis infection in Guinea pigs. Antimicrob Agents Chemother 2011;55(1): 124–31. [DOI] [PMC free article] [PubMed] [Google Scholar]
16. Tasneen R, Li SY, Peloquin CA, et al. Sterilizing activity of novel TMC207- and PA-824-containing regimens in a murine model of tuberculosis. Antimicrob Agents Chemother 2011;55(12):5485–92. [DOI] [PMC free article] [PubMed] [Google Scholar]
17. Ibrahim M, Andries K, Lounis N, et al. Synergistic activity of R207910 combined with pyrazinamide against murine tuberculosis. Antimicrob Agents Chemother 2007;51(3):1011–5. [DOI] [PMC free article] [PubMed] [Google Scholar]
18. Andries K, Gevers T, Lounis N. Bactericidal potencies of new regimens are not predictive of their sterilizing potencies in a murine model of tuberculosis. Antimicrob Agents Chemother 2010;54(11): 4540–4. [DOI] [PMC free article] [PubMed] [Google Scholar]
19. Li S-Y, Tasneen R, Tyagi S, et al. Bactericidal and sterilizing activity of a novel regimen with bedaquiline, pretomanid, moxifloxacin, and pyrazinamide in a murine model of tuberculosis. Antimicrob Agents Chemother 2017;61(9):1–8. [DOI] [PMC free article] [PubMed] [Google Scholar]

20. FDA. SIRTURO® (bedaquiline) tablets, for oral use highlights of prescribing information 2012. Available at: https://www.sirturo.com/sites/default/files/pdf/sirturo-pi.pdf. Accessed January 13, 2019.
21. van Heeswijk RPG, Dannemann B, Hoetelmans RMW. Bedaquiline: a review of human pharmacokinetics and drug-drug interactions. J Antimicrob Chemother 2014;69(9):2310–8. [DOI] [PubMed] [Google Scholar]
22. Diacon AH, Donald PR, Pym A, et al. Randomized pilot trial of eight weeks of bedaquiline (TMC207) treatment for multidrug-resistant tuberculosis: long-term outcome, tolerability, and effect on emergence of drug resistance. Antimicrob Agents Chemother 2012;56(6):3271–6. [DOI] [PMC free article] [PubMed] [Google Scholar]
23. Rouan MC, Lounis N, Gevers T, et al. Pharmacokinetics and pharmacodynamics of TMC207 and its N-desmethyl metabolite in a murine model of tuberculosis. Antimicrob Agents Chemother 2012; 56(3):1444–51. [DOI] [PMC free article] [PubMed] [Google Scholar]
24. McLeay SC, Vis P, Van Heeswijk RPG, et al. Population pharmacokinetics of bedaquiline (TMC207), a novel antituberculosis drug. Antimicrob Agents Chemother 2014;58(9):5315–24. [DOI] [PMC free article] [PubMed] [Google Scholar]
25. Svensson EM, Dosne AG, Karlsson MO. Population pharmacokinetics of bedaquiline and metabolite M2 in patients with drug-resistant tuberculosis: the effect of time-varying weight and albumin. CPT Pharmacometrics Syst Pharmacol 2016; 5(12):682–91. [DOI] [PMC free article] [PubMed] [Google Scholar]
26. Svensson EM, Murray S, Karlsson MO, et al. Rifampicin and rifapentine significantly reduce concentrations of bedaquiline, a new anti-TB drug. J Antimicrob Chemother 2014;70(4): 1106–14. [DOI] [PMC free article] [PubMed] [Google Scholar]
27. Svensson EM, Aweeka F, Park JG, et al. Model-based estimates of the effects of efavirenz on bedaquiline pharmacokinetics and suggested dose adjustments for patients coinfected with HIV and tuberculosis. Antimicrob Agents Chemother 2013; 57(6):2780–7. [DOI] [PMC free article] [PubMed] [Google Scholar]
28. Brill MJE, Svensson EM, Pandie M, et al. Confirming model-predicted pharmacokinetic interactions between bedaquiline and lopinavir/ritonavir or nevirapine in patients with HIV and drug-resistant tuberculosis. Int J Antimicrob Agents 2017;49(2): 212–7. [DOI] [PubMed] [Google Scholar]
29. Huitric E, Verhasselt P, Koul A, et al. Rates and mechanisms of resistance development in Mycobacterium tuberculosis to a novel diarylquinoline ATP synthase inhibitor. Antimicrob Agents Chemother 2010;54(3):1022–8. [DOI] [PMC free article] [PubMed] [Google Scholar]
30. Hartkoorn RC, Uplekar S, Cole ST. Cross-resistance between clofazimine and bedaquiline through upregulation of mmpl5 in mycobacterium tuberculosis. Antimicrob Agents Chemother 2014; 58(5):2979–81. [DOI] [PMC free article] [PubMed] [Google Scholar]
31. Almeida D, Ioerger T, Tyagi S, et al. Mutations in pepQ confer low-level resistance to bedaquiline and clofazimine in Mycobacterium tuberculosis. Antimicrob Agents Chemother 2016;60(8):4590–9. [DOI] [PMC free article] [PubMed] [Google Scholar]
32. Villellas C, Coeck N, Meehan CJ, et al. Unexpected high prevalence of resistance-associated Rv0678 variants in MDR-TB patients without documented prior use of clofazimine or bedaquiline. J Antimicrob Chemother 2017;72(3):684–90. [DOI] [PMC free article] [PubMed] [Google Scholar]
33. Bloemberg GV, Keller PM, Stucki D, et al. Acquired resistance to bedaquiline and delamanid in therapy for tuberculosis. N Engl J Med 2015;373(20): 1986–8. [DOI] [PMC free article] [PubMed] [Google Scholar]
34. World Health Organization (WHO). WHO technical report on critical concentrations for TB drug susceptibility testing of medicines used in the treatment of drug-resistant TB. Geneva (Switzerland): WHO; 2018. . Available at: http://www.who.int/tb/publications/2018/WHO_technical_report_concentrations_TB_drug_susceptibility/en/. [Google Scholar]

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